BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,981	06/27/2001	Roland Gerritsen van der Hoop	01722906	3783

7590 02/08/2002

Joseph A. Mahoney
Mayer, Brown & PlaTT
P.O. Box 2828
Chicago, IL 60690

EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/892,981	VAN DER HOOP, ROLAND GERRITSEN	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29 and 45-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29 and 45-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election without traverse of the invention of Group I, claims 1-29 and 45-73 in Paper No. 5 received January 17, 2002 is acknowledged.

Claims 30-44 are cancelled in Paper No. 5 received January 17, 2002.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-29, 45-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "non-orally deliverable pharmaceutically acceptable steroids" in claims 1 and 45 renders the claims indefinite as to what steroid compounds are encompassed by the claims.

The expression "menopause disorders" in claims 1 and 45 renders the claims indefinite as to the disorders or conditions encompassed thereby. The instant specification, page 21, line 8-16 attempt to define the expression "menopause disorders"; however, it is not clear what peri-menopausal conditions, which is encompassed by the expression "menopause disorders", are encompassed by the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was

made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-29 and 45-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rubin (US Patent 5,5059,603), Ebert et al. (US Patent 5,152,997), and Place (US Patent 6,117,446) in view of Langtry et al. (Drugs 1999; 57(6): 967-989), Remington's Pharmaceutical Sciences (1990, 18th ed., pages 1305 and 1314), Merck Index (11th ed., 1989, page 821, monograph 5103), Hofman et al. (US Patent 4,563,473), and Atkinson et al. (US Patent 4,442,094).

Rubin teaches methyl testosterone is useful in a method of treating androgen deficiency associated disorders such as impotence (See particularly col. 2, line 59 - col. 3, line 11).

Ebert et al. teaches testosterone therapy is a useful in a method of treating male hypogonadism and the conditions associated male hypogonadism comprising employing a matrix containing testosterone and penetration enhancer onto the skin (See col. 1, line 20-66).

Place teaches a method of hormonal replacement therapy and symptoms thereof such as female sexual dysfunction and vaginal dryness comprising a treatment of a woman with an estrogen such as estradiol and an androgenic steroid such as testosterone (See col. 11, line 6-61). Place also teaches that the dosage of the estradiol may be 0.05 to 0.5 mg (See col. 11, line 36-61). Place also teaches that the dosage of the androgenic agent such as testosterone to be 0.1 to 2.5mg (See col. 11, line 36-61).

The references do not expressly teach the dosage form of the instant invention to be a gel comprising isopropyl myristate, ethanol, and Carbopol. The references do not

expressly teach the employment of the composition containing the combination of testosterone and methyltestosterone or the combination of estradiol and methyltestosterone. The references do not expressly the dosage of methyltestosterone to be 0.2 mg to about 50.0mg and that of testosterone or estradiol to be 0.1g to about 100.0g. The references do not teach the employment of sildenafil in the method herein.

Langtry et al. teaches that sildenafil is useful to treat erectile dysfunction (See abstract).

Remington's Pharmaceutical Sciences teaches that ethanol is a commonly used pharmaceutical solvent (See page 1314-1315). Remington's Pharmaceutical Sciences also teaches that carbopol is a commonly used pharmaceutical excipient as thickening agent (See page 1305).

Merck Index teaches that Isopropyl myristate is useful in topical pharmaceutical preparation where good penetration through skin is desired (See page 821, col. 1).

Hofman et al. teaches that ethanol, Carbopol, and Isopropyl myristate are typical agents for formulating gel (See col. 2, line 19-35).

Atkinson et al. teaches that ethanol, Carbopol, and Isopropyl myristate are typical agents for formulating gel (See col. 4, line 64 – col. 5, line 42).

It would have been obvious to one skill in the art when the invention was made to employ a gel formulation comprising sildenafil and the actives, estradiol and methyltestosterone or testosterone and methyltestosterone, in the dosage herein and ethanol, Carbopol, and Isopropyl myristate as the excipients in a method of treating menopausal disorders in a mammal.

One of ordinary skill in the art would have motivated to employ a gel formulation comprising sildenafil and the actives, estradiol and methyltestosterone or testosterone and methyltestosterone, in the dosage herein and ethanol, Carbopol, and Isopropyl myristate as the excipients in a method of treating menopausal disorders in a mammal because estradiol, testosterone, and methyltestosterone are all known in the art to be useful in method of treating both male and female menopausal disorders. Employing two of these agents which are known to be useful to treat menopausal disorders individually into a single method useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. Employing sildenafil with testosterone and methyltestosterone, which are known to be useful in treating impotence individually, in a method useful for the very same purpose would be *prima facie* obvious. Furthermore, the optimization of result effect parameters (e.g., dosage range of the active) is obvious as being within the skill of the artisan. Moreover, interchanging the dosage form of the menopausal disorder treating composition into a gel preparation and employing common excipients in the same is within the purview of skilled artisan.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
February 6, 2002

MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600